

U.S. Patent Application Serial No. 09/883,394
Amendment dated February 10, 2004
Reply to OA of November 17, 2003

IN THE CLAIMS:

Please amend claims 6-13, 27-32 and 36 as follows:

Claim 1 (Withdrawn): A polypeptide having 4 to 20 tyrosine sulfate residues.

Claim 2 (Withdrawn): A polypeptide according to Claim 1, wherein each sulfate residue is bound to a reactive group in a tyrosine residue constituting the polypeptide.

Claim 3 (Withdrawn): A polypeptide represented by the formula:



wherein m is an integer of 4 to 30; 4 to 20 of R's are tyrosine sulfate residues, and the rest of R's are, the same or different, an amino acid residue having no strong acid residue, each reactive group in each side chain of the amino acid residue being able to be protected; A is a hydrogen atom, a protective group of N-terminus or an acid residue derived from a strong acid; and B is a hydroxyl group or a protective group of C-terminus.

Claim 4 (Withdrawn): A polypeptide represented by the formula:



wherein R¹'s are, the same or different, independently an amino acid residue introducing a strong

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acid residue thereinto via a reactive group of the amino acid residue; m is an integer of 3 to 30; A is a hydrogen atom, a protective group of N-terminus or an acid residue derived from a strong acid; and B is a hydroxyl group or a protective group of C-terminus.

Claim 5 (Withdrawn): A polypeptide according to Claim 3, which is represented by the formula:



wherein m' is an integer of 4 to 20; R³ is a tyrosine sulfate residue; each R² is an amino acid residue having no strong acid residue; each reactive group in each side chain of the amino acid residue being able to be protected; n is an integer of 1 to 26; and A and B are as defined in Claim 3.

Claim 6 (Withdrawn): A ~~combined~~ reaction product of (a) a maleimide compound containing a polypeptide having 3 to 30 acid residues derived from a strong acid having a pKa of 3 or less and (b) a substance having affinity for an analyte to be measured in a sample of body fluids or cells.

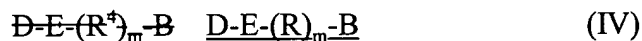
Claim 7 (Currently Amended): A compound comprising a polypeptide having 3 to 30 acid residues derived from a strong acid, which is an acid having a pKa of 3 or lower, the N-terminus of

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which is the polypeptide being bound through a spacer to a maleimido group.

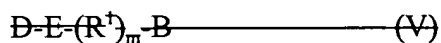
Claim 8 (Withdrawn): A ~~combined reaction~~ product of according to claim 6, wherein the maleimide compound is the compound of Claim 7 and a the substance having affinity is a compound having a SH group and affinity for an analyte to be measured in a sample of body fluids or cells.

Claim 9 (Currently Amended): A compound according to claim 7, which is represented by the formula:



wherein D is a maleimido group; E is a spacer; m is an integer of 3 to 30; at least three ~~R^t's~~ R's are, the same or different, independently an amino acid residue introducing strong acid residue therein the via a reactive group of the amino acid residue, and the rest of ~~R^t's~~ R's are, the same or different, an amino acid residue having no strong acid residue, each reactive group in each side chain of the amino acid residue being able to be protected; and B is a hydroxyl group or a protective group of C-terminus.

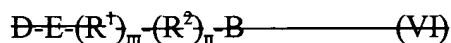
Claim 10 (Withdrawn): A compound according to claim 7, which is represented by the formula:



wherein D is a maleimido group; E is a spacer; m is a spacer; ~~R¹'s~~ at least R's are, the same or different, independently an amino acid residue introducing a strong acid residue therein via a reactive group of the amino acid residue; ~~m is an integer of 3 to 30~~ and the rest of R's are, the same or different, an amino acid residue having no strong acid residue, each reactive group in each side chain of the amino acid residue being able to be protected; and B is hydroxyl group or a protective group of C-terminus,

wherein the amount of amino acid residue having no strong acid residue can be zero.

Claim 11 (Withdrawn): A compound according to claim 7, which is represented by the formula:



wherein D is a maleimido group; E is a spacer; m is an integer of 3 to 30; ~~R¹'s~~ at least three R's are, the same or different, independently an amino acid residue introducing a strong acid residue therein via a reactive group of the amino acid residue, ~~each R² is~~ and the rest of R's are, the same or different, an amino acid residue having no strong acid residue, each reactive group in each side chain of the amino acid residue being able to be protected; ~~n' is an integer of 1 to 27~~; and B is a hydroxyl

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group or a protective group of C-terminus,

wherein the amino acid residue having no strong acid residue is present in a number of an integer of 1 to 27, while m is an integer of 3 to 30.

Claim 12 (Withdrawn): A reagent for measuring an analyte to be measured in a sample of body fluids or cells, which comprises a ~~combined~~ reaction product of Claim 6.

Claim 13 (Withdrawn): A reagent for measuring an analyte to be measured in a sample of body fluids or cells, which comprises a ~~combined~~ reaction product of Claim 8.

Claims 14 - 21 (Canceled).

Claim 22 (Withdrawn): The polypeptide according to claim 3, which is Ala-(Tyr(SO₃H))₄-β Ala (SEQ ID NO:11), Ala-(Tyr(SO₃H))₄ (SEQ ID NO: 12), Ala-(Tyr(SO₃H))₅-β Ala (SEQ ID NO:13), Ala-(Tyr(SO₃H))₅ (SEQ ID NO:14), Ala-(Tyr(SO₃H))₇-β Ala (SEQ ID NO: 15), Ala-(Tyr(SO₃H))₇ (SEQ ID NO:16), Ala-(Tyr(SO₃H))₈-β Ala (SEQ ID NO:17), Ala-(Tyr(SO₃H))₈ (SEQ ID NO:18), or Ala-(Tyr(SO₃H))₁₀-β Ala (SEQ ID NO:19).

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Claim 23 (Withdrawn): The polypeptide according to claim 4, which is $(\text{Ser}-(\text{SO}_3\text{H}))_8-$
 $(\text{Tyr}(\text{SO}_3\text{H}))_5$ (SEQ ID NO:21).

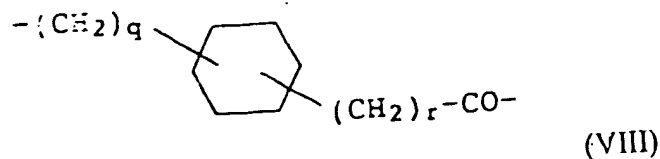
Claim 24 (Withdrawn): The polypeptide according to claim 5, which is $\text{Ala}-(\text{Tyr}(\text{SO}_3\text{H}))_4$
(SEQ ID NO:12), $\text{Ala}-(\text{Tyr}(\text{SO}_3\text{H}))_5$ (SEQ ID NO:14), $\text{Ala}-(\text{Tyr}(\text{SO}_3\text{H}))_7$ (SEQ ID NO:16) or $\text{Ala}-$
 $(\text{Tyr}(\text{SO}_3\text{H}))_8$ (SEQ ID NO:18).

Claim 25 (Previously Presented): The polypeptide according to claim 7, which is 4-
maleimidobutyl-Ala-(Tyr(PO_3H_2))₅-β Ala (SEQ ID NO:18).

Claim 26 (Previously Presented): The combined product according to claim 7, wherein the
spacer is a group represented by the following formula (VII), (VIII) or (IX):

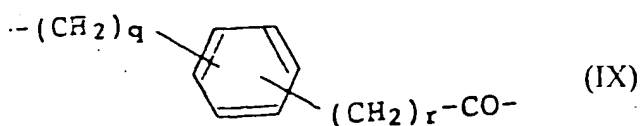


wherein p is an integer of 1 to 10,



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wherein each of q and r is zero or an integer of 1 to 5,



wherein q and r are as defined above.

Claim 27 (Withdrawn): A combined reaction product according to claim 6, wherein the strong acid has a pKa of 3 or lower.

Claim 28 (Withdrawn): A combined reaction product according to claim 6, wherein the strong acid is sulfuric acid or phosphoric acid.

Claim 29 (Withdrawn): A combined reaction product according to claim 6, wherein the polypeptide has four or more acid residues derived from a strong acid.

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Claim 30 (Withdrawn): A ~~combined~~ reaction product according to claim 6, wherein the polypeptide has four or more acid residues derive from a strong acid.

Claim 31 (Withdrawn): A ~~combined~~ reaction product according to claim 6, wherein the total number of the amino acid residues of the polypeptide is 3 to 30.

Claim 32 (Withdrawn): A ~~combined~~ reaction product according to claim 6, wherein the substance is an antibody, an antigen, a pectin, an inhibitor for an enzyme, a polynucleotide chain complementary to single-stranded polynucleotide of a nucleic acid or a receptor for thyroid-stimulating hormone.

Claim 33 (canceled).

Claim 34 (Previously Presented): A compound according to claim 7, wherein the strong acid is sulfuric acid or phosphoric acid.

Claim 35 (Previously Presented): A compound according to claim 7, wherein the amino acid residue introducing a strong acid therein is serine, threonine or tyrosine.

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Claim 36 (Withdrawn): A ~~combined~~ reaction product according to claim 8, wherein the substance having a SH group is an antibody Fab'.